Claims

1. A process for the manufacture of tert-butyl (E)-(6-{2-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]vinyl}-(4R,6S)-2,2-dimethyl[1,3]dioxan-4-yl)acetate which comprises reaction of diphenyl [4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-ylmethyl]phosphine oxide with tert-butyl 2-[(4R,6S)-6-formyl-2,2-dimethyl-1,3-dioxan-4-yl]acetate in the presence of a strong base.

2. A process as claimed in claim 1 wherein the reaction is carried out at a temperature in the range of -20°C to -90°C.

3. A process as claimed in claim 1 or 2 wherein the strong base is sodium bis(trimethylsilyl)amide.

4. A process as claimed in claim 1, 2 or 3 wherein the reaction is carried out in a solvent selected from tetrahydrofuran, dimethoxyethane and toluene, and mixtures thereof.

5. A process as claimed in any of claims 1 to 4 wherein 1.0 to 1.2 equivalents of base are used per equivalent of the phosphine oxide.

6. A process as claimed in any of claims 1 to 5 wherein 1.0 to 1.35 equivalents of tert-butyl 2-[(4R,6S)-6-formyl-2,2-dimethyl-1,3-dioxan-4-yl]acetate are used per equivalent of the phosphine oxide.

7. The compound diphenyl [4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-ylmethyl]phosphine oxide.

8. The compound tert-butyl (E)-(6-{2-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]vinyl}-(4R,6S)-2,2-dimethyl[1,3]dioxan-4-yl)acetate.

9. A process for the manufacture of a compound of the formula IV

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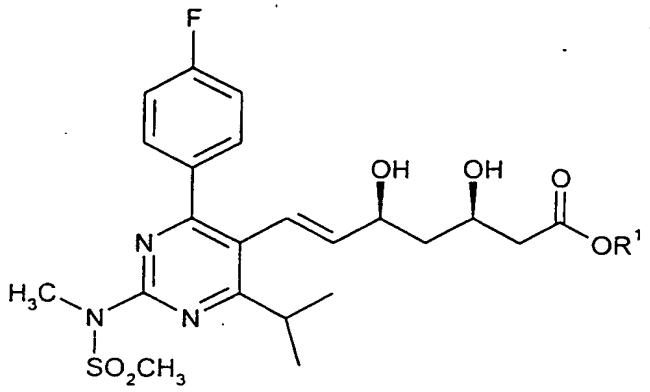


Formula IV

in which R^1 is hydrogen or a pharmaceutically acceptable cation which comprises

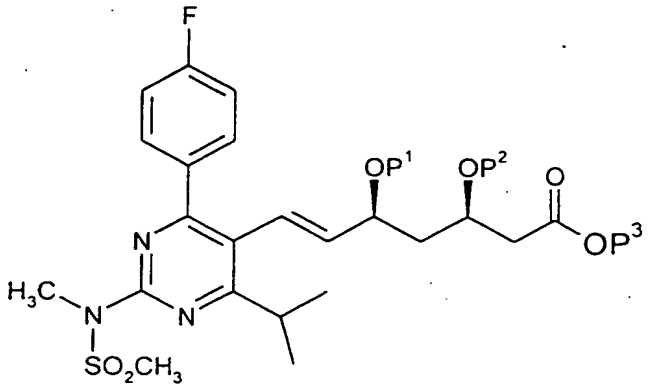
(1) reaction of diphenyl [4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-ylmethyl]phosphine oxide with tert-butyl 2-[(4R, 6S)-6-formyl-2,2-dimethyl-1,3-dioxan-4-yl]acetate in the presence of a strong base to give tert-butyl (E)-(6-{2-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]-pyrimidin-5-yl]vinyl}(4R,6S)-2,2-dimethyl[1,3]dioxan-4-yl)acetate of formula I;

(2) cleavage of the dihydroxy protecting group from the product of step (1);

(3) cleavage of the tert-butyl ester group under basic conditions from the product of step (2) to form a compound of the formula IV in which R^1 is a pharmaceutically acceptable cation;

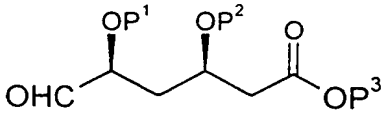
optionally followed by neutralisation to give a compound of the formula IV in which R^1 is hydrogen; and/or optionally followed by conversion to another compound of the formula IV in which R^1 is a pharmaceutically acceptable cation.

10. A process for the manufacture of a compound of the formula VI



Formula VI

which comprises reaction of diphenyl [4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-ylmethyl]phosphine oxide with a compound of the formula V



Formula V

in the presence of a strong base, wherein P^1 and P^2 are alcohol protecting groups, or P^1 and P^2 taken together is a 1,3-diol protecting group, and P^3 is a carboxylic acid protecting group.